REMARKS

The present application is submitted in reply to the non-final office action dated March 18, 2011 ("Office Action").

Applicant has amended claim 1 to more distinctly claim the subject matter he deems as his invention. Support for this amendment can be found in the Specification, page 22, lines 14 and 15; page 24, lines 3-13; page 27, lines 4-10; page 28, lines 23-25; pages 29 and 30, Table 3; and page 30, lines 1 to 14; page 34, line 8; pages 34 and 35, Table 4; and original claim 2. In addition, Applicant has added new claims 24-31. Support for new claim 24 appears in the Specification, page 22, lines 16-18.[1] Support for new claims 25-31 can be found in claims 7-13, respectively. Finally, Applicant has cancelled claims 2, 4, and 17-23. Claims 5 and 6 were previously cancelled.

Upon entry of the proposed amendments, claims 1, 3, 7-16, and 24-31 will be pending. Among them, claims 3, 7-10, 12, 13, 25-28, 30, and 31 have been withdrawn and claims 1, 11, 14-16, 24, and 29 are for examination. Applicant respectfully requests that the Examiner reconsider this application in view of the following remarks.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1 and 22-23 for indefiniteness. See the Office Action, page 2, last paragraph. She asserts that it is not clear what therapeutic gains (1)-(6) recited in claims 22 and 23 refer to. See the Office Action, page 3, lines 1-3. Applicant has cancelled claims 22 and 23 and amended claim 1, from which claims 22 and 23 depend, to remove the term "therapeutic gain." These claim amendments have rendered the rejection moot.

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[1] The recitation "cancer-free" in this new claim is fully supported by the Specification. More specifically, as shown in the Specification, an animal model, used in radiation experiments of Examples 3-8, 10, and 13, was cancer-free. See page 22, lines 16-19. Note that the added language to an amended claim does not have to be set forth verbatim in the specification. The Federal Circuit, in reversing a Board's 35 U.S.C. § 112, first paragraph rejection, held that there was adequate written description support for applicant's claim limitation, despite the fact that it was not set forth "*in haec verba*" (i.e., "in these words" or "verbatim") in the specification. See *In re Wright*, 9 USPQ2d 1649 (Fed. Cir. 1989).

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects claims 1, 2, 4, 11, 14-17, 22, and 23 for failing to comply with the written description requirement. See the Office Action, page 3, third paragraph, lines 1 and 2. More specifically, the Examiner asserts that Applicant failed to provide any guidance in his response as to where support can be found for the limitations added to claim 1. See the Office Action, page 3, last paragraph, lines 2 and 3. In this response, some of these added limitations have been removed in this response. To provide clear guidance as to the support for the limitations that remain in claim 1, other than pointing out above the support for these limitations, Applicant also specify below the location(s) where each and every of these limitations appears:

"reducing radiation-induced normal tissue damage in a subject"	Specification, page 22, lines 14 and 15; and page 28, lines 23-25
"more inflammatory cell infiltration"	Specification, page 27, lines 7 and 8; page 30, lines 9 and 10; and page 30, Table 3
"desquamation"	Specification, page 24, line 6; page 30, lines 3 and 4; and page 30, Table 3
"dermatitis"	Specification, page 24, line 6
"mucositis"	Specification, page 34, line 8; and pages 34 and 35, Table 4
"epidermal atrophy"	Specification, page 30, line 5; and page 30, Table 3
"tissue fibrosis"	Specification, page 24, line 7
"ulceration"	Specification, page 24, line 7; page 27, line 7; page 30, line 9; and page 30, Table 3
"tissue necrosis"	Specification, page 24, line 7; page 27, line 7; page 30, line 9; and page 30, Table 3
"bulla formation"	Specification, page 27, line 7; page 30, line 9; and page 30, Table 3
"plantar-palmar syndrome"	Original claim 2
"reduced epithelium thickness"	Specification, page 24, line 9; page 30, line 6; and page 30, Table 3
"increased dermis thickness"	Specification, page 24, lines 9 and 10; page 30, line 8; and page 30, Table 3

"more vessel density"	Specification, page 30, line 7; and page 30, Table 3
"increased collagen deposition"	Specification, page 24, line 11; page 30, line 7; and page 30, Table 3

In view of the above remarks, Applicant respectfully submits that the ground for this rejection has been removed.

Rejection under 35 U.S.C. § 102

The Examiner rejects claims 1, 2, 4, 11, 14-16, 22, and 23 for lack of novelty over Samid, US Patent 5,877,213 ("Samid"). See the Office Action, page 5, second paragraph. Applicant respectfully traverses.

Note that, as claims 2, 4, 22, and 23 have been cancelled, only claims 1, 11, and 14-16, as well as new claims 24 and 29, are at issue.

Claim 1 will be discussed first. This claim, as amended, is drawn to a method for reducing radiation-induced normal tissue damage with a histone hyperacetylating agent, e.g., phenylbutyrate. Examples of the radiation-induced normal tissue damage include desquamation, dermatitis, mucositis, epidermal atrophy, fibrosis, ulceration, tissue necrosis, bulla formation, and plantar-palmar syndrome.

The Examiner correctly points out that Samid teaches a method of treating and preventing cancer with phenylacetic acid and its derivatives, e.g., phenylbutyrate. See the Office Action, page 5, third paragraph, lines 1-5. According to the Examiner, Samid "also teaches a method of treating cancer with sodium phenylbutyrate concomitantly or in combination with conventional radiotherapy." Below Applicant will refer to the combined therapy as "the Samid method." See the Office Action, page 5, third paragraph, lines 5-7. Further, it is the Examiner's position that "the administration of ... sodium phenylbutyrate to patients undergoing chemotherapy or radiotherapy is expected to ... [reduce radiation-induced damage as required by claim 1], whether recognized by the author or not" on the basis that "products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstance or, in the present case, the same host [i.e., cancer patient]." See the Office Action, page 6,

lines 4-8. In other words, this rejection is based on the Examiner's assertion that the subject to be treated by the method of claim 1 is the same as that by the Samid method.

Applicant would like to point out that the patentability of amended claim 1 does not reside in the subject to be treated. Rather, it resides at least in reduction of radiation-induced normal tissue damage with a histone hyperacetylating agent, which is not taught or even suggested in Samid. Of note, claim 1, as amended, now recites "reducing radiation-induced normal tissue damage."

In view of the above remarks, Applicant submits that claim 1, as amended, is novel over Samid.

So are claims 11, 14-16, 24 and 29, all of which depend from claim 1.

Further, claim 24, as well as claim 29, dependent therefrom, requires that the target of the claimed method be a cancer-free subject. For example, the cancer-free subject can be a person exposed to radiation in a nuclear power plant accident. By contrast, the Samid method is used to treat cancer patients. On this second and independent ground, both claims 24 and 29 are not anticipated by Samid.

Rejection under 35 U.S.C. § 103

The Examiner rejects claims 1, 2, 4, 11, 14-17, 22, and 23 for obviousness over Samid in view of Shufeng et al., 2002, Investigational New Drugs, 20, 281-295 ("Shufeng"). See the Office Action, pages 6 and 7, carryover paragraph. Applicant respectfully traverses.

Only claims 1, 11, 14-16, 24, and 29 are at issue. Again, claim 1 will be addressed first. It covers a method of reducing radiation-induced normal tissue damage with phenylbutyrate.

As discussed above, Samid does not teach claim 1. Further, it is commonly known in the art that treating cancer is to promote cell death and, on the other hand, reducing radiation-induced normal tissue damage is to reduce cell death. To the extent that Samid teaches promoting cell death with phenylbutyrate, it would have led a skilled artisan away from claim 1, which, as discussed above, covers reducing death of normal

cells with phenylbutyrate. In any event, Samid fails to suggest reducing radiation-induced normal tissue damage with phenylbutyrate, which is required by claim 1.

Shufeng does not cure this deficiency. This reference, as correctly pointed out by the Examiner, teaches DMXAA as an investigational anti-cancer drug and as a biological response modifier. It does not mention "phenylbutyrate" as recited in claim 1, nor "[reduction of] radiation-induced normal tissue damage" as also recited in claim 1.

In view of the above remarks, Applicant submits that Samid and Shufeng, taken alone or in combination, do not render claim 1 obvious.

Nor do they render obvious claims 11, 14-16, 24 and 29, all of which depend from claim 1.

Withdrawn Claims

In the restriction requirement dated December 19, 2006, the Examiner required election of one of the histone hyperacetylating agents, asserting that those agents are independent and distinct. In response, Applicants elected sodium phenylbutyrate as a single species.

In this Office Action, the Examiner has considered claims 1-2, 4, 11, 14-17, and 22-23, which read on this elected species, and withdrawn claims 3, 7-10, 12, 13, and 18-21, which read on the non-elected species. See the Office Action, page 2, lines 11-13.

Applicants would like to bring to the Examiner's attention a rule set forth in 37 CFR § 1.141, which is reproduced below:

> Two or more independent and distinct inventions may not be claimed in one national application, except that **more than one species of an invention** [] may be specifically claimed in different claims in one national application, provided the application also includes an **allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form** [] (emphases added).

Clearly, this rule requires that the Examiner also consider non-elected species claims, after a generic claim has been held to be allowable.

Turning to this application, independent claim 1, citing the general term "histone hyperacetylating agent," is generic to the species recited in dependent claims 7-10, 12, and 13 and dependent new claims 25-28, 30, and 31. As discussed above, generic claim 1 is allowable. Pursuant to the above-quoted rule, the Examiner should also consider the non-elected histone hyperacetylating agent species recited in claims 7-10, 12, and 13 and new dependent claims 25-28, 30, and 31, all of which are dependent from the generic claim.

Applicants submit that, for at least the reasons that claim 1 is allowable, the withdrawn claims dependent therefrom, including claims 7-10, 12, and 13 and new claims 25-28, 30, and 31, are also allowable. It is therefore requested that the Examiner allow these claims.

CONCLUSION

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment.

In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed.

Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

No fee is believed to be due. Please apply any other charges or credits to Deposit Account No. 50-4189, referencing Attorney Docket No. 55701-004002.

Respectfully submitted,

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